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# A Review of the Phytochemistry and Pharmacology of *Lannea* species

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ABSTRACT

The *Lannea* species belong to the Anacardiaceae family and are widely distributed throughout the world. Members of this species have been used traditionally to treat stomach ache, seminal weakness, excessive seminal emissions, ulcers, sore injuries, dyspepsia, gout, dysentery, sore eyes, leprosy, sprains and bruises, diarrhea, gastritis, rheumatic pain, sterility, scurvy, epilepsy and intestinal helminthiasis and hematochezia. In traditional medicine, some members of this species are used as astringent, while the leaf extract of some plants of this species are used in treating inflammations, sprains and body pain. The juice extracted from the leaves of plants belonging to this species are taken orally to treat toothache while their stem bark is made into a paste and used to treat body pains. The *Lannea* species are used as antidote in coma caused by narcotics and to stop bleeding and prevent tetanus. Phytochemical investigations of the *Lannea* species have revealed that many chemical constituents from this family are highly bioactive. Although, the medicinal properties of *Lannea* species are recognized worldwide, there is no review article on the phytochemical constituents and pharmacological activities of the *Lannea* species. The present paper reviews the medicinal properties alongside with peculiar phytoconstituent, biological activity, isolated compounds and pharmacological activities of various plants of the *Lannea* species. The medicinal properties of these plants could be attributed to the availability of a broad range of bioactive constituents such as flavonoids, phenolic acids, terpenoids (monoterpenes, sesquiterpenes, diterpenes, and triterpenes) and sterols reported in this species.

***Keywords:*** Pharmacology, Anacardiaceae, *Lannea*, phytochemistry, antioxidant.

## Introduction

Historically, many plants have been used by traditional medicine practitioners as their primary source of treatment of diseases.[1] Due to the abundance of bioactive principles present in plants and the remarkable medicinal properties, they have been used extensively in traditional medicine practice, for example the traditional systems of Indian medicine like Ayurveda, Siddha and Unani.[2] Some of these plants have been traditionally proved to possess pharmacological activities, but many have not been scientifically justified.[3] Members of the *Lannea* genus belonging to the family Anacardiaceae, have been studied extensively for their chemical constituents and pharmacological activities. They have gained importance due to their remarkable variations biological activities and uses in traditional medicine. A number of researchers attempted to justify the ethnomedicinal claims of this genus and succeeded in proving some.[4] Still many of the traditional uses of this plant are devoid of a recorded scientific proof. The aim of this paper is to review exhaustively the phytochemistry, pharmacology and medicinal importance of all plants of the *Lannea* genus.

*Distribution and Morphology*

The genus *Lannea* constitutes about 40 species of trees, shrubs, and undershrubs. They are widely distributed in Africa, but only one species, *Lannea coromandelica* (Houtt.) Merr., is located in tropical Asia.[5] Members of this genus are small deciduous tree that grow up to 14 m tall. Their leaves are usually 5-7 cm wide and opposite with acute tip, they are covered by velvet hair when young. The flowers are unisexual and green in colour. The flowers possess four broad ovate sepals which are about 1 mm long. The petals are four in number, they are 2 mm long, and oblong and greenish yellow in colour with the stamens twice the number of petals. The petals turn into yellow at the time of maturation. The tree flowers in months between February and April. Its Fruits occur as drupes, which are dull red to pink in colour. The fruiting season is between May to July. The tree when injured exudes a brown gum that turns black on drying.[6]

## Methodology

The major scientific databases including SciFinder, Sciencedirect, Medline and Google Scholar were queried for information on *Lannea* genus using various keyword combinations. The International Plant Name Index was also used to verify the names of species and authors.

### Folklore claims

*Lannea coromandelica* twigs are used as tooth sticks, the bark is used for skin diseases, the tender leaves and roots are used for stomach ache in India and roots in used in breweries by *Gadaba* people of India.[7] Its fruits are crushed and mixed with water and is used as fish poison.[8] The stem bark of *Lannea coromandelica* is used to treat sexual ailments[9]. The decoction and macerated extracts of the leaves and bark of the plant is taken orally to treat injuries and hematochezia.[10] It has also been claimed to be used as antidote in coma caused by narcotics, to treat dyspepsia, gout, dysentery, sore eyes, leprosy, sprains and bruises[11]. The plant bark is being used as a bandage to treat bone fracture by *Lambada* tribes of India.[11] In folklore medicine, *Lannea coromandelica*

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gum is soaked in water, rubbed on stone and applied locally to treat pain. The inner bark of stem is crushed, and the juice is squeezed over cuts to stop bleeding and to prevent tetanus.[12,13]

*Lannea kerstingii* stem bark decoction is used by many women during pregnancy or during lactation in Togo to treat anaemia and malaria.[14] In West African countries such as Ivory coast, *L. kerstingii* stem bark and root are consumed as traditional remedies for the treatment of diarrhoea, gastritis, rheumatism, sterility, scurvy, epilepsy and intestinal helminthiasis.[15] In Benin, *L. kerstingii* leaves are used in the treatment of ulcer.[16] Pharmacological studies of *L. kerstingii* extracts have revealed several properties such as antihelmintic, antimicrobial, trypanocidal and acetylcholinesterase inhibitory properties.[17,18]

*Lannea microcarpa*, commonly known as African grape, is widely distributed in the sub-Saharan region from Senegal to Cameroon. Traditional remedies prepared from its leaves, bark, roots and fruits are used to treat mouth blisters, rheumatism, sore throats, dysentery, conjunctivitis, stomatitis, skin eruptions, and ulcers.[19] *Lannea barteri* stem bark and roots are consumed by natives from Northern Côte d'Ivoire, as traditional remedies for the treatment of diarrhea, gastritis, rheumatism, sterility, intestinal helminthiasis, oedema, rickets, wounds, scurvy and epilepsy.[20] In Traditional African Medicine (TAM), *Lannea welwitschii* is used for treating swellings, oedema, gout, hemorrhoids and emesis.[21]

## Phytochemistry

*Phytochemical screening*

The phytochemical screening of extracts of *L. humilis* and *L. barteri* was found to contain steroids, tannins, flavonoids, alkaloids, saponins, triterpenoids and saponins.[22-23] *Lannea coromendelical* bark extracts contained flavonoids, sugar, protein, triterpenoids, alkaloids, tannins and phenols.[24] Chemical investigation revealed the presence of oils, reducing sugars, alkaloids, saponins, tannins and anthraquinones in the aqueous bark extract of *Lannea welwitschii*.[21] The ethyl acetate fraction of the leaves of *L. kerstingii* was found to contain only flavonoids and tannins. While the petroleum ether extract contains only steroids and triterpenes.[25] The preliminary phytochemical investigation of the leaves extracts of *L. coromandelica* revealed the presence of terpenes, carbohydrates, glycosides, alkaloids, flavonoids, fats, oils, waxes and tannins.[26] 4'-methoxymyricetin 3-*O*-*α*-L-rhamnopyranoside, myricetin (3-*O*-*α*-L-rh), amnopyranoside, myricetin 3-*O*-*β*-D-glucopyranoside, vitexin, isovitexin, gallic acid, and epicatechin have been identified as major constituents of the leaf extracts of *Lannea microcarpa*.[27]

The crude alcoholic extract of flowers of *L. coromandelica* contained Isoquercitrin (I). The leaves of *L. coromandelica* were proven to contain ß-Sitosterol (II), Physcion (III), Quercetin (IV), Leucocyanidin (V) and Leucodelphinidin (VI).[28] Dihydroflavonols, (2R,3S)-(+)-3',5-dihydroxy-4',7-dimethoxydihydroavflonol (VII)and (2R,3R)-(+)-4',5,7 trimethoxydihydroflavonol (VIII) were isolated from the stem bark of *Lannea coromandelica*, along with the known (2R,3R)-(+)-4',7- di-O-methyldihydroquercetin (IX), (2R,3R)-(+)-4',7-di-O-methyldihydrokaempferol and (2R,3R)-(+)-4'-O methyl dihydro quercetin (X).[29] Morin (XI), a flavonoid aglycone was also isolated from the plant and the possible structure was identified as 3,5,7,2',4'-OH-flavone.[30] Polyflavonoid tannin have been reported to be present in *L. coromandelica*.[31] Four flavonoids named as 6,7-(2'',2''-dimethyl chromeno)-8-g,g-dimethyl allyl flavanone (XII), 3',4'dihydroxy-7,8 (2'',2''-dimethyl chromeno)-6-g,g dimethyl allyl flavono (XIII), l, 7-methyltectorigenin,(XIV) and Irisolidone (XV) have been isolated from leaves of *Lannea acida* (Figure 1).[32]

## Physico-chemical Analysis

The percentage composition of ash in *Lannea microcarpa* seeds was report to be 3.11%.[33] The physicochemical properties of the oil was also reported as; refractive index (1.473), melting point (22.60°C), saponification value (194.23 mg of KOH/g of oil), iodine value (61.33 g of $I_2$/100 g of oil), acid value (1.21 mg of KOH/g of oil) peroxide value (1.48 meq of $O_2$/kg of oil) and oxidative stability index (43.20 h).[33]

## Pharmacology of *Lannea* species

*Wound healing activity*

Ethanol and acetone extract of *Lannea coromandelica* (Houtt) Merr bark when applied to male wistar rats in the form of simple ointments exhibited wound healing activity in excision and incision methods. Framycetin sulphate was taken as standard for both methods. The ethanolic and acetone extracts gave 97.11% and 95.95% activity respectively in excision method and showed sustainable results in incision method.[34]

*Antibacterial activity*

The antibacterial activity of fractions of the stem bark of *Lannea humilis* displayed antibacterial actions against some selected bacteria viz: *B. subtilis, P. mirabilis, S. aureus, K pneumonia, S. pyogenes* and *S. typhi* and *E. coli*, with zone of inhibition from 12 – 27 mm. Combinations of the fractions of *Lannea humilis* with ciprofloxacin produced synergistic effect with zone of inhibition between 21 and 41 mm. The minimum inhibitory concentration and minimum bactericidal concentration of the standard antibiotics (6.25 and 12.5 mg/mL, respectively) was essentially reduced (to 0.75 and 1.5 mg/mL, respectively) when the fractions were used in combination with the standard antibiotic ciprofloxacin.[35] The leaf extract of *Lannea Kerstingii* were found to be active against *S. aureus, S. faecalis, B. subtilis*, MRSA, *E. coli, K. pneumonia, S. dysentariae* and the fungus *C. tropicalis*.[25] *Lannea coromandelica* bark extract showed moderate activity against *Staphylococcus aureus, Salmonella typhi, Shigella dysenteriae, Pseudomonas aeruginosa and Escherichia coli*.[36] The antimicrobial activity of three members of the *Lannea* genus (*Lannea velutina, Lannea acida* and *Lannea microcarpa*) was investigated;[37] *Bacillus subtilis and Enterobacter aerogenes* showed sensitivity to all the three plants. *Staphyloccoccus aureus* was more sensitive to *Lannea microcarpa* while *Salmonella typhyrium* was more sensitive to *L. velutina*. The results of antibacterial screening revealed that *L. barteri* inhibited the growth of some selected bacteria. Antimicrobial screening of *L. barteri* extracts showed bactericidal and bacteriostatic activities, with minimum inhibitory concentration (MIC) values ranging between 47 and 375 µg/mL against *Fusarium oxysporum* f. sp. *vasinfectum* and *Fusarium oxysporum* f. sp. *Lycopersici*.[23] The stem root and bark extracts of *Lannea barteri* showed activity against bacteria and fungi. Antimicrobial screening with minimum inhibitory concentration (MIC) values ranging between 47 and 375 µg/mL.[20] The ethanol and acetone extracts of the stem bark of *L. coromandelica* were investigated for the antibacterial activity against *B. cereus* MTCC430, *S. aureus, E. coli, P. vulgaris* and *A. niger*. The plant showed antibacterial activity and the zone of inhibition was found to be 20, 26, 13, 12 and 21 mm respectively for ethanolic extract and 19, 22, 14, 11 and 22 mm respectively for acetone extract.[34]

*Total Phenolic and Flavonoid Contents*

Majumder *et al.*[36] reported the total extractable phenolic contents of methanol extract of *Lannea coromandelica* bark extract to be 93.03 ± 0.21 mgGAE/g plant extract. The total phenolic compounds was 38.04 mgGAE/g for *L.velutina*, 40.07 mgGAE/g for *L. microcarpa* and 40.55 mgGAE/g for *L. acida* . The total flavonoid content expressed in quercetin Equivalents varied between 6.45 mg/g for *L. microcarpa* to 8.70 mg/g for *L. acida* and 11.02 mg/g for *L. velutina*.[37]

*Antioxidant activity*

The antioxidant activity of *L. humili*s stem bark extracts demonstrated a dose-dependent increment. The ethyl acetate extract displayed most noteworthy antioxidant activity of 98% at 240 µg/mL, followed by the hexane extract which had a percentage antioxidant activity of 92% at 240 µg/mL.[35] The methanol extract demonstrated percentage antioxidant activity of 71% at 240 µg/mL. *Lannea acida* barks extracts demonstrated the highest antioxidant activity of 90% among the threes plant extract with a good ability of scavenging 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical. This activity correlated with the high quantity of total phenolic content[37]. *Lannea coromandelica* gave radical scavenging activity (RAS) ranging between 58.5 - 91.4% for both roots and stem bark.[20] The DPPH radical scavenging activity of *Lannea coromandelica* extracts was found to be concentration dependent with half maximal inhibitory concentration ($IC_{50}$) values of 12.12 ± 0.16 µg/mL, while half maximal inhibitory concentration ($IC_{50}$) values of standard ascorbic acid was found to be

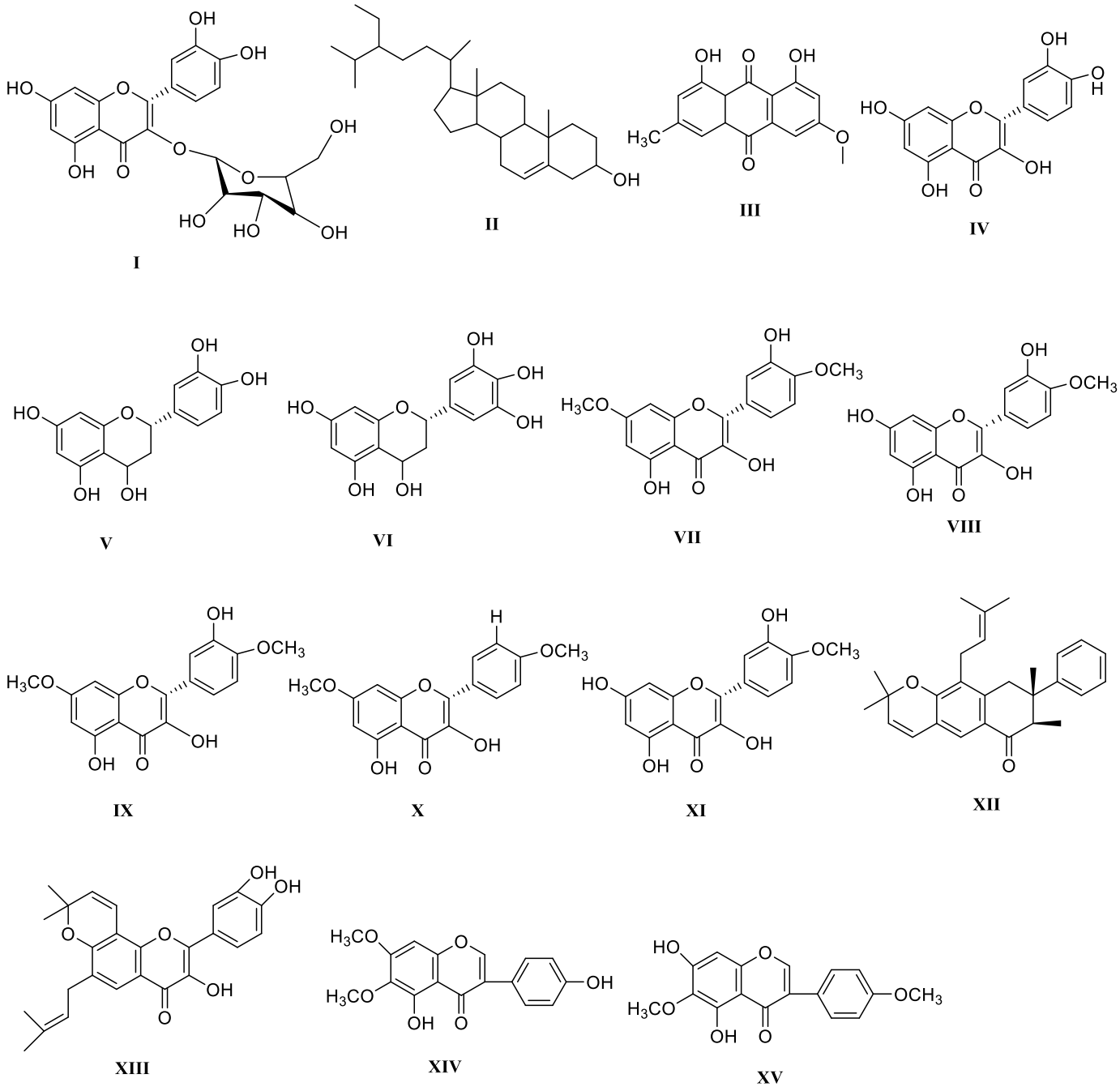


**Figure 1:** Chemical structures of phytoconstituents isolated from *Lannea* species.

12.22 ± 0.11 µg/mL. The *L. acida* barks extract exhibited half maximal inhibitory concentration ($IC_{50}$) of 345.72 ± 7.76 µg/mL while half maximal inhibitory concentration ($IC_{50}$) of 478 ± 8.55 was recorderd for *L. velutina* and half maximal inhibitory concentration ($IC_{50}$) values 450.33 ± 36.03 for *L. microcarpa.* The highest amount of phenolic compounds were found in *Lannea acida* (40.55 ± 0.26 g GAE/100g). A half maximal inhibitory concentration ($IC_{50}$) value was observed as (83.28 ±2.12) µg/mL, for 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity of *L. coromandelica*. The ethanolic extract and hydroalcoholic bark extract of the plant showed a potential antioxidant activity which may be due to the presence of phenolic groups, terpenoids and alkaloids.[38] The inhibition of the total reactive oxygen species (ROS) generation of extract of *L. coromendelica* was also found to be concentration dependent with $IC_{50}$ values of 13.73 ±0.48 µg/mL, while $IC_{50}$ values of standard trolox was found to be 8.66 0.11µg/mL.[25] In the 2,2-diphenyl-1-picrylhydrazyl (DPPH) test, dichloromethane and methanol extracts of stem bark and root of *Lannea barteri*, showed significant percentage inhibition activities. Their activities seem to be similar for both roots and stem bark.[20] Important concentrations of phenolic compounds with strong antioxidant capacities have been found in the fruit of *Lannea microcarpa* (1005.75 mg/100 g of fruit).[39]

*Analgesic activity*

The tail withdrawal reflex time following administration of methanol extract of *Lannea coromandelica* bark extract showed statistically significant ($p < 0.05$ - 0.001) analgesic activity when compared to the reference drug Nalbuphine.[26]

*Antidiarrhea activity*

Majumder *et al.*[36] reported that the oral administration of *L. coromandelica* bark extract significantly inhibited response induced by acetic acid in a dose dependent manner when compared with the untreated controls. At a dose of 200 mg/kg, the methanol bark extract of *L. coromandelica* showed significant ($p < 0.05$) 68.86% reduction in the number of fecal episodes, whereas loperamide offered 89.14% protection.[36] Oral administration of castor oil produced intestinal fluid volume of 2.33 ± 0.17 mL, the aqueous bark extract of *Lannea*

*welwitschii* at 400 mg/kg significantly ($p < 0.05$) reduced the volume of intestinal fluid to 1.40 ± 0.25.[22]

*Cytotoxicity activity*
The crude extract of *L. coromandelical* (twig) showed high cytotoxicity (307.12 ± 15.97) against the HepG2 cells; an effect that was significantly different to that of melphalan ($P = 0.023$).[40] *L. kerstingii* hydroalcohol extract and its aqueous extract showed a similar toxicityvalue of $IC_{50}$ 102 and 104 µg/mL respectively, but with the neutral red assay, *L. kerstingii* hydroalcohol extract ($IC_{50}$, 29 µg/mL) was found to be more toxic than its aqueous extract ($IC_{50}$:141 µg/mL).[18] The hydroalcohol extract of *L. kerstingii* (500 µg/mL) and its aqueous extract significantly increased *malondialdehyde* (MDA) levels.[18]

*Hypotensive activity*
The ethanolic extract of the *Lannea coromandelica* administered to anesthetized dogs (5-100 mg/kg) and rats (1-25 mg/kg) intravenously showed a reduction in the arterial blood pressure of the animals.[41]

*Anticonvulsant screening*
*Lannea barteri* (160 mg/kg) significantly ($p \leq 0.05$) delayed the mean onset of seizures induced by Pentylenetetrazole PTZ when compared with normal saline treated group. Similarly, the extract at 160 mg/kg significantly ($p \leq 0.05$) prolonged the latency of convulsion induced by strychnine nitrate STN. *Lannea barteri* (40 mg/kg) significantly ($p \leq 0.05$) delayed the mean onset of seizures induced by picrotoxin in mice.[42]

## Conclusion

The *Lannea* species are of vast and significant medicinal importance. As it is reviewed in this paper, they have shown significant antioxidant, antidiarrhea, antimicrobial, analgesic, wound healing and hepatoprotective activities. This may be due to availability of the phytochemicals as well as high content of flavonoids and phenolic compounds present in these species. This shows that members of the species could serve as a source of antibiotics, antioxidants and bioactive compounds or as starting materials for the synthesis of modern pharmaceuticals used for treatment of human and animal diseases.

## Conflict of interest

The authors declare no conflict of interest.

## Author's Declaration

The author hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by him.

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